

PENICILLIN



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MANUFACTURING CHEMISTS
EST. 1849
FINE CHEMICALS

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PENICILLIN, useful in the treatment of many previously resistant infections, is obtained from the culture liquor of the mold *Penicillium notatum* when grown under suitable conditions. It is a fugitive material, decomposing in alkaline or acid solutions or when exposed to moderate heat, but is powerfully bacteriostatic, to some extent bactericidal and of very low toxicity. Its neutral salts are reasonably stable, especially when kept dry and cold.

For clinical use the sodium salt of penicillin is supplied in the form of an amorphous light yellow or brown powder, hermetically sealed in sterile glass ampuls. These may be stored without appreciable loss of activity of the contents if kept below 5° c. Penicillin is very soluble. Solutions for parenteral use should be made with pyrogen-free distilled water, normal saline

or 5% glucose solution, and should be used while fresh, as they tend to lose activity on standing.

Since it has not yet been possible to separate penicillin completely from other substances present in the culture liquor, available preparations vary somewhat in composition. By using especially high doses it has sometimes been possible to show a certain degree of toxicity, but the therapeutic ratio of the penicillin preparations now available is very high, and the largest doses given for curative purposes have never produced serious toxic effects. As an extra precaution preparations offered for medicinal use must give a negative modified U. S. P. pyrogen test.

CLINICAL INDICATIONS

WHILE of very broad applicability, penicillin is in general most active against Gram-positive organisms of the

type of *Staphylococcus*, *Pneumococcus* and hemolytic *Streptococcus*. It is compatible with the normal defense mechanisms of the animal body and in dilute solution does not destroy the leucocytes nor delay tissue regeneration. Its activity may persist in spite of pus, blood, serum or the products of tissue destruction and is almost independent of the number of microorganisms present. Penicillin is effective in the treatment of gonococcal and meningococcal infections and may effect cures with sulfonamide-resistant strains of both types. However, until a more adequate supply of penicillin becomes available, its use in gonorrhea should be limited to the comparatively small proportion of cases that are found resistant to the sulfonamides.

In certain types of focal infections penicillin has not yet given an encouraging proportion of cures. Pending further investigation it should not be used in

the treatment of bacterial endocarditis. On the other hand, osteomyelitis has been successfully treated.

As in all curative treatments, primary dependence must be placed upon the body's natural defenses, and maintenance of the general condition is especially important in penicillin therapy. Optimum nutrition and vitamin balance must be maintained, and such supplemental therapy as blood transfusion is often necessary in critical cases.

DOSAGE and ADMINISTRATION

SINCE penicillin has not yet been isolated as a pure chemical, it is necessary to measure the potency of each preparation. This is recorded in terms of an arbitrary "Oxford unit" proposed by the British group which first developed penicillin. The minimum amount of penicillin customarily given an adult is 5,000 Oxford

units. Much larger amounts have been administered without injury to the patient. The use of insufficiently large doses or the lapse of too long an interval between doses involves a certain risk of making the infection penicillin-resistant.

On account of the rapidity with which penicillin is eliminated, the continuous intravenous drip method of administration presents important advantages. In the absence of cardiac involvement, a rate of up to 40 drops of solution per minute has been found permissible. In 24 hours the amount given may exceed 100,000 Oxford units. Since the method is exceptionally efficient, a more common dosage is 30,000 to 40,000 units per 24 hours.

When an intermittent procedure is preferred, severe infections are usually treated with initial intravenous doses of 15,000 to 20,000 units every three hours.

After three or four days the usual procedure is to diminish the dosage to 5,000 units every four hours intramuscularly.

Penicillin is so soluble that 10,000 units or more may be dissolved in one cubic centimeter of the diluent. Patients experience a slight burning at the site of injection.

In meningitis cases, both intrathecal and intramuscular (or intravenous) treatments are used. Rarely more than 5,000 units every 24 hours intrathecally are given in parallel with the customary intramuscular or intravenous dose.

Infected wounds and burns may be successfully treated solely by parenteral administration of penicillin, but additional local administration is often desirable. A satisfactory procedure is to apply gauze soaked in the penicillin solution and cover by a protective

bandage. Fresh penicillin should be supplied at least once a day. As it must be recognized that not all organisms will be inhibited, determination by culture of the bacteria present is a necessary adjunct to penicillin treatment of such injuries. In cases of infection with hemolytic streptococci some English workers have used with good results a penicillin cream made by emulsification of the solution with oil and wax.

GENERAL CONSIDERATIONS

PENICILLIN PFIZER is packed dry in ampuls containing various multiples of the 5,000-unit dose. It should be stored at temperatures below 5°C. (41° F.).

In solution penicillin is not stable even at pH value of 7.0 and temperature of 0° C. Decomposition is accelerated at body temperature. This factor merits consideration when calculating the desired frequency of

administration. It is also of importance that penicillin is very rapidly eliminated through the kidneys, so that even in the absence of decomposition, the concentration in the blood tends to fall rapidly.

As penicillin solutions, especially those containing glucose, may support the growth of molds and some bacteria, all containers, tubing and other equipment should be sterilized before use and frequently replaced, using a sterile technique throughout. Penicillin solutions cannot endure heat sterilization. If any degree of contamination is suspected, they should be freed from microorganisms by passage through a sterile Seitz filter.

